

Variant: *NM_000277.3(PAH):c.1001G>C (p.Cys334Ser)*

Version: 2.0

CA229263 [↗](#)

102464 (ClinVar) [↗](#)

Gene: PAH ([HGNC:5053](#))

Condition: phenylketonuria ([MONDO:0009861](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: bffa79b5-d67a-4083-b12e-2d5e84071018

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HGVS expressions

NM_000277.3(PAH):c.1001G>C (p.Cys334Ser)

NM_000277.3:c.1001G>C

NC_000012.12:g.102844400C>G

CM000674.2:g.102844400C>G

NC_000012.11:g.103238178C>G

CM000674.1:g.103238178C>G

NC_000012.10:g.101762308C>G

NG_008690.1:g.78203G>C

NG_008690.2:g.119011G>C

ENST00000553106.6:c.1001G>C

ENST00000307000.7:c.986G>C

ENST00000549247.6:n.760G>C

ENST00000551114.2:n.663G>C

ENST00000553106.5:c.1001G>C

ENST00000635477.1:c.105G>C

ENST00000635528.1:n.516G>C

NM_000277.1:c.1001G>C

NM_000277.2:c.1001G>C

NM_001354304.1:c.1001G>C

NM_001354304.2:c.1001G>C

Likely Pathogenic

Met criteria codes **4**

PM3_Supporting

PP3_Strong

PP4

PM2_Supporting

Not Met criteria codes **1**

PM5

Evidence Links **0**

Expert Panel

Phenylketonuria VCEP [↗](#)

Criteria Specification Information

[↗](#) **Criteria Specification:** ClinGen Phenylketonuria Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for PAH Version 2.0.0

[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.1001G>C (p.Cys334Ser) variant in PAH has been reported in 2 patients with mild PKU/HPA. (BH4 deficiency not ruled out. PMID: 8632937, 10693064). It was detected with pathogenic variant p.F299C (unknown phase). This variant is absent from controls in ExAC, gnomAD, 1000 Genomes, and ESP. A deleterious effect is predicted in SIFT, Polyphen-2, MutationTaster, and REVEL=0.976. In summary, this variant meets criteria to be classified as Likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PM2_supporting, PP3_strong, PP4, PM3_supporting.

Met criteria codes

PM3_Supporting			Detected with F299C (P, 5 submitters), parental analysis not reported
PP3_Strong			Predicted deleterious in SIFT, PolyPhen2, MutationTaster. REVEL=0.976.
PP4			Detected in multiple patients with mild PKU/HPA. BH4 deficiency not ruled out. PMID: 8632937, 10693064
PM2_Supporting			Absent from controls in ExAC, gnomAD, 1000 Genomes, ESP

Not Met criteria codes

PM5			The current variant is the only missense variant found in this codon in ClinVar.
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Curation History

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